IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	van Lengerich	
Serial No.	:	Rule 1.53 Divisional Application Of U.S. S.N. 09/269,763 Filed: April 12, 1999	Prior Group Art Unit: 1732
Filed	:	Concurrently Herewith	Prior Examiner: Mark Eashoo
Title	:	EMBEDDING AND ENCAPSULATION OF CONTROLLED RELEASE PARTICLES	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

With reference to the above-identified patent application, please amend the application prior to issuance of the first Office Action.

IN THE SPECIFICATION:

On page 1, before "FIELD OF THE INVENTION", please insert the following new paragraph:

--This application is a Divisional of U.S. Application Serial No. 09/269,763, filed April 12, 1999, which is a 371 of PCT/US97/18984 filed October 27, 1997, which claims priority of U. S. serial no. 60/052,717, filed July 16, 1997, and U. S. serial no. 60/029,038, filed October 28, 1996.--

Please amend the paragraph bridging pages 7 and 8 as follows:

The present invention provides a continuous process for producing controlled release, discrete, solid particles which contain an encapsulated and/or embedded component. The particles comprise a matrix material in which the active component is encapsulated or embedded. The matrix material is plasticized upon heating to form a melt. The active component is admixed with the melt without substantially deleteriously affecting or decomposing the encapsulant or the matrix material. The active component is admixed with the plasticized matrix material at low temperatures and under low shear mixing conditions to thereby avoid substantial destruction of or volatilization of active components. Additionally, high water contents may be employed so as to substantially reduce viscosity and facilitate substantial gelatinization of the starch without substantially destroying the starch molecules. Subsequent removal of at least part of the water prior to adding the encapsulant avoids excessive drying or evaporation of the plasticizing liquid which may adversely affect the encapsulant content. The moisture reduction within the extruder also provides for the attainment of a formable composition capable of being formed into discrete, substantially uniform pieces. Extrusion of the matrix and active component blend may be performed without substantial expansion of the product thereby providing a high density product which is less susceptible to attack by aqueous or oxygen-containing mediums thereby providing a prolonged release time. The process of

the present invention may be used to encapsulate heat sensitive components or readily oxidizable components, for example, pharmaceutically or biologically or nutritionally active components, without substantially destroying their activity. The products of the present invention may be edible for direct consumption or for incorporation into food products. In other embodiments of the invention, products, such as chemical or agricultural products such as pesticides, herbicides, fungicides, insecticides, rodenticides, or other products like detergents or flavorants, fragrances, and the like may be advantageously embedded or encapsulated to control or delay their release from their surrounding matrix.

On page 37 please amend the last full paragraph as follows:

The last 2 to 3 l/d screw length may be used to generate sufficient pressure to extrude the material through the die openings. The die used comprised 20 openings, arranged in two circles of ten bores, each having a cylindrical bore of 2 mm over a length of 4 mm and a subsequent narrow opening of 1 mm over a land length of 2 mm. The larger opening of the first part of the dies is critical to prevent substantial energy dissipation within the die through overshearing that would result in an increase of the product temperature and thus cause a thermal destruction of the encapsulant. Additionally, too narrow die channels cause higher pressures before the die and may

result in overheating of the product in the last barrel despite the cooling. The product temperature of the matrix at the encapsulant feeding point was about 25°C. The product temperature at the exit die was 52°C. The pressure at the die was 80 bar. The mean residence time of the encapsulant from the feed location to the die exit was about 35 seconds. On a calculated basis, the maximum flow rate of extrudate per die area is 0.361 kg/hr per mm^2, based upon the total amount of components added to the extrudate.

On page 38, please amend the second full paragraph as follows:

In this example, the effect of addition of the encapsulant prior to and after heat treatment was evaluated. The extruder used was the same as used in Example 1 and screw rpm was 150. A blend of 99.7% by weight starch with 0.3% GMS was fed at 4.0 kg/hr into barrel #1. Vegetable oil was fed at a rate of 0.39 kg/h into barrel #1. Ascorbic acid was fed at a rate of 1.15 kg/h into barrel 1 (Comparative Example 1) and was exposed to the following barrel temperature profile: Barrel 1 (15°C), Barrel 2 (15°C), Barrel 3 (120°C), Barrel 4 (140°C), Barrel 5 (140°C), Barrel 6 (15°C), Barrel 7 (15°C), Barrel 8 (15°C), Barrel 9 (15°C). On a calculated basis, the maximum flow rate of extrudate per die area is 0.352 kg/hr per mm^2, based upon the total amount of components added to the extruder. Analysis of ascorbic acid after extrusion resulted in a 72.3% loss.

On page 39 please amend the first full paragraph as follows:

In this example, a heat-sensitive fat soluble component was encapsulated. The extruder used was the same as used in Example 1 and the screw rpm was 150. A blend of 96.7% by weight starch, 3% by weight LDPE and 0.3% by weight GMS was fed at 4.0 kg/hr into barrel #1. Vegetable oil was fed at a rate of 0.16 kg/h into barrel #1. Following barrel temperature profile was used: Barrel 1 (15°C), Barrel 2 (15°C), Barrel 3 (120°C), Barrel 4 (140°C), Barrel 5 (140°C), Barrel 6 (15°C), Barrel 7 (15°C), Barrel 8 (15°C), Barrel 9 (15°C). The encapsulant salicylic acid may be fed at a rate of 1.15 kg/h into barrel 7 at a temperature of 20°C. The encapsulant was mixed into the matrix and extruded into ropes that were cut at the die into distinct spherical pellets having a diameter of about 1 mm. On a calculated basis the maximum flow rate of extrudate per die area is 0.338 kg/hr per mm^2 , based upon the total amount of components added to the extruder. After extrusion, the extruded pellets were dried at 30°C for about 12 hours to a final moisture content of approximately 8% by weight. The dried pellets were stable in water for 16 hours and the salicylic acid may be sufficiently encapsulated within the matrix to allow controlled release under appropriate conditions.

IN THE CLAIMS:

As indicated in the Request for Filing a Divisional Application, cancel original claims 1-24. Claims 25-89 are added in the original filing of the present divisional application but they were not present in parent application 09/269,763.

REMARKS

A "Version with Markings to Show Changes Made to Parent Application No. 09/269,763" is attached.

The specification has been amended to incorporate the priority data.

As in the parent application, the specification has been amended at page 7, line 16, to correct an inadvertent error. The amendment is supported, for example, by the context of page 7, lines 13-20 and at page 6, lines 6-13, page 23, line 24 to page 24, line 19 and page 55, lines 17-20. The specification has also been amended, as in the parent application, to provide the calculated maximum throughput or rate of extrudate per die area for examples 1, 2 and 3. All of the variables needed for calculating the maximum rates, such as number and diameter of the die openings and the total feed rate, are given in each example for which the extrudate rate per die area is added. The rate of extrudate per die area is calculated as the total flow rate of all components added divided by the total area of all circular openings. Thus, in Example 1, the total flow rate is the sum of the flow rates of the blend of corn starch with LLPE and GMS (4 kg/hr), vegetable oil (0.17 kg/hr), water (1.1 kg/hr) and acetylstyrene (0.4 kg/hr) and is equal to 5.67 kg/h. The total die area for 20 openings each 1 mm in diameter is 20 x[(½)^{2}x3.14)] = 15.7 mm^2. Thus, the calculated maximum flow rate per die area for 5.67 kg/hr total flow rate is equal to 5.67/15.7=0.361 kg/hr per mm^2 for Example 1. The actual flow rate per die area is lower

than the maximum flow rate calculated due to removal of some amounts of water from the heated extruder barrels. Similarly, in Examples 2 and 3 the calculated maximum flow rates per die area are 0.352 kg/hr per mm^2 (5.54/15.7=0.352) and 0.338 kg/hr per mm^2 (5.31/15.7=0.338).

In the Request for filing the divisional application, original claims 1-24 have been cancelled without prejudice or disclaimer. Claims 25-89 were not originally filed with parent application no. 09/269,763. Claims 25-89 are included in the original filing of the present divisional application. Claims 25-89 do not introduce new matter.

Support for new claims 25-89 is as follows:

Support for new claim 25 can be found, for example, in the instant specification at page 7, lines 1-15, page 11, lines 1-15, page 12, lines 15-19, page 27, lines 9-27, page 28, line 30 to page 29 line 10, and at page 39, lines 11-13, and by original claim 1;

support for new claims 26 and 53 can be found in the instant specification, for example, at page 11, line 27 to page 12, line 4, and at page 29, lines 10-11;

support for new claims 27, 29, 54 and 57 can be found, for example, in the instant specification at page 21, lines 20-24;

support for new claims 28 and 55 can be found, for example, in the instant specification at page 27, lines 4-8;

support for new claims 30-31and 58-59 can be found, for example, in the instant specification at page 13, lines 3-16;

support for new claims 32-33 and 60 can be found, for example, in the instant specification at page 13, lines 17-29;

support for new claims 34 and 61 can be found, for example, in the instant specification at page 29, lines 11-13;

support for new claims 35 and 62 can be found, for example, in the instant specification at page 9, line 26 to page 10, line 2, and page 29 lines 4-5;

support for new claims 36, 43, 63 and 71 can be found, for example, in the instant specification at page 14, line 9 to page 21, line 10;

support for new claims 37 and 64 is provided, for example, at page 9, lines 16-18, page 26, lines 30-31, and page 29, lines 9-10;

support for new claims 38 and 65 is provided, for example, at page 9, lines 8-11;

support for new claims 39 and 81is provided, for example, at page 12, lines 15-19, page 14, lines 4-8, and page 21, lines 15-19;

support for new claims 40 and 67 is provided, for example, at page 28, line 30 to page 29 line 6;

support for new claims 41 and 68 is provided, for example, in the paragraph bridging pages ll and 12, and at page 13, lines 24-30, and page 42 lines 1-2

and 10-19;

support for new claims 42 and 70 can be found, for example, in the instant specification at page 12, lines 3-4;

support for new claims 44-45, 49, 72, 74 and 78 is provided, for example, at page 6, line 17 to page 7, line 2, page 7, line 27 to page 8, line 1, page 11, lines 19-23, page 14, lines 9-19, and page 35, lines 1-13;

support for new claims 46, 75, 82, and 85 is provided, for example, in the instant specification at page 14, lines 9-26 and at page 21, lines 8-10;

support for new claims 47 and 76 is provided, for example, in the instant specification at page 14, lines 27-29;

support for new claims 48 and 77 is provided, for example, in the instant specification at page 11, lines 19-26 and at page 35, lines 1-13;

support for new claims 50 and 79 is provided, for example, in the instant specification at page 11, line 27 to page 12, line 14;

support for new claims 51 and 80 is provided, for example, in the instant specification at page 6, line 28 to page 7, line 2, and page 11, lines 19-23;

support for new claims 52, 69, and 83-89 can be found, for example, in the instant specification at page 7, lines 1-15, page 11, lines 1-15, page 11, line 27 to page 12, line 4, page 13 line 24 to page 14 line 3, page 23, lines 12-14, page 27, lines 9-27, page 28 line 30 to page 29, line 10, page 33, lines 17-20, page 39, lines 11-13, and

page 42, lines 1-25, and original claim 1 and Fig. 3;

support for new claim 56 is provided, for example, at page 28 lines 30-31;

support for new claim 66 can be found, for example, in the instant specification at page 10, lines 7-11, and page 14, lines 4-8; and

support for new claim 73 can be found, for example, in the instant specification at page 28, line 30 to page 29, line 4.

No new matter is added by the above amendment. Upon entry of the Preliminary Amendment, claims 25-89 will stand pending in the instant application.

Please take the cancellation of original claims 1-24 into account before calculating the filing fee.

If any additional fees are due, please charge our Deposit Account No. 501032.

Respectfully submitted,

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February 13, 2001

Attachment: "Version with Markings to Show Changes Made to Parent Application No. 09/269,763"

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capable of being formed into discrete, substantially uniform pieces. Extrusion of the matrix and active component blend may be performed without substantial expansion of the product thereby providing a high density product which is less susceptible to attack by aqueous or oxygen-containing mediums thereby providing a prolonged release time. The process of the present invention may be used to encapsulate heat sensitive components or readily oxidizable components, for example, pharmaceutically or biologically or nutritionally active components, without substantially destroying their activity. The products of the present invention may be edible for direct consumption or for incorporation into food products. In other embodiments of the invention, products, such as chemical or agricultural products such as pesticides, herbicides, fungicides, insecticides, rodenticides, or other products like detergents or flavorants, fragrances, and the like may be advantageously embedded or encapsulated to control or delay their release from their surrounding matrix.

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